

FIGURE 1

A: BoNTA(H_c) synthetic gene (Version #1) SEQ ID NO: 1

GAATTCGAAACGatgCGTCTGCTGTCTACCTTCACTGAATAACATCAAGAAC
ATCATCAATAACCTCCATCCTGAACCTCGCCTACGAATCCAATCACCTGAT
CGACCTGCTCGCTACGCTTCCAAAATCAACATCGTTCTAAAGTTAACT
TCGATCCGATCGACAAGAACATCAGATCCAGCTGTTCAATCTGGAATCTTCC
AAAATCGAAGTTATCCTGAAGAACATGCTATCGTATAACAACACTATGTACG
AAAACCTCTCCACCTCCTCTGGATCCGTATCCGAAATACCTCAACTCC
ATCTCTGAAACAATGAATAACACCATCATCAACTGCATGGAAAACAATT
CTGGTTGGAAAGTATCTCTGAACACTACGGTGAATCATCTGGACTCTGCAG
GACACTCAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGA
TCAACATCTCTGACTACATCAATCGCTGGATCTCGTACCATCACCAAC
AATCGTCTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACC
AGAAACCGATCTCAATCTGGTAACATCCACCGCTTCTAATAACATCATG
TTCAAACCTGGACGTTGTCGTGACACTCACCGCTACATCTGGATCAAATA
CTTCAATCTGTTGACAAAGAACACTGAACGAAAAAGAAATCAAAGACCTG
TACGACAACCAGTCCAATTCTGGTATCCTGAAAGACTCTGGGGTGAECT
CCTGCAGTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAAC
AAATACGTTGACGTCAACAATGTAGGTATCCGGGTTACATGTACCTGA
AAGGTCCCGTGGTCTGTTATGACTACCAACATCTACCTGAACCTTCC
CTGTACCGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACA
AGGACAATATCGTCGCAACAATGATCGTGTATACATCAATGTTAGTT
AAGAACAAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTAG
AAAAGATCTGTCGCTCTGGAAATCCGGACGTTGGTAATCTGTCTCAG
GTAGTTGTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCA
AAATGAATCTGCAGGACAACAATGGTAACGATATCGGTTCATCGGTT
CCACCAGTTCAACAATATCGCTAAACTGGTTGCTTCCAACGGTACAATC
GTCAGATCGAACGTTCTCTCGCACTCTGGGTTGCTCTGGAGTTCATC
CCGGTTGATGACGGTTGGGTGAACGTCCGCTGtaaGAATT

B: BoNTA(H_c) encoded protein (Version #1) SEQ ID NO: 2

MRLLSFTFEYIKNIINTSILNLRYESNHLIDLRYASKINIGSKVNFDPIDKNQI
QLFNLESSKIEVILKNAIVYNSMYENFSTSFWRIPKYFNSISLNNEYTIINCME
NNSGWKVSLNYGEIWTQDTQEQIKQRVVFYKYSQMINISDYINRWIFVTITNN
RLNNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRHYIWIKYFNLF
DKELNEKEIKDLYDNQNSNSGILKDFWGDYLQYDKPYMLNLYDPNKYVDV
NNVGIRGYMYLKGPRGSVMTNIYLNSSLYRGTKFIKKYASGNKDNIVRN
NDRVYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQLVVVMKSKN
DQGITNKCKMNLQDNNGNDIGFIGFHQFNIAKLVASNWYNRQIERSRTL
GCSWEFIPVDDGWGERPL*

FIGURE 2

A: BoNTA(H_c) synthetic gene (version #2) SEQ ID NO: 3

GAATTCGAAACGatgTCTACCTTCACTGAATAACATCAAGAACATCATCAAT
ACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCTGTC
TCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACITCGATCCGA
TCGACAAGAACATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAATCGA
AGTTATCCTGAAGAACATGCTATCGTATACAACACTCTATGTACGAAAACCTCT
CCACCTCCTCTGGATCCGTATCCGAAATACTTCAACTCCATCTCTG
AACAAATGAATAACACCATCATCAACTGCATGGAAAACAATTCTGGTTGGA
AAGTATCTCTGAACATACGGTGAACATCTGGACTCTGCAGGACACTCA
GGAAATCAAACAGCGTTGTATTCAAATACTCTCAGATGATCAACATCT
CTGACTACATCAATCGCTGGATCTCGTACCATACCAACAATCGTCTG
ATAAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAACCGA
TCTCCAATCTGGTAACATCCACGCTTCTAATAACATCATGTTCAAACCTG
GACGGTTGTCGTGACACTCACCCTACATCTGGATCAAATACTCAATCT
GTTCGACAAAGAACATGAACGAAAAAGAAATCAAAGACCTGTACGACAA
CCAGTCCAATTCTGGTATCCTGAAAGACTCTGGGGTGAACACCTGCAGT
ACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATACGT
TGACGTCAACAATGTAGGTATCCCGGTTACATGTACCTGAAAGGTCCG
CGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTCCCTGTACCG
TGGTACCAAAATTCAATCATCAAGAAATACGCGTCTGGTAACAAGGACAAT
ATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTTAGTTAAGAACAA
AGAATACCGTCTGGCTACCAATGCTCTCAGGCTGGTAGAAAAGATC
TTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCAGGTAGTTGT
AATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGAAT
CTGCAGGACAACAATGGTAACGATATCGGTTCATCGGTTCCACCAAGTT
CAACAATATCGCTAACTGGTTCTCCAACGGTACAATCGTCAGATCG
AACGTTCCCTCTCGCACTCTGGTTGCTCTGGAGTTCAACCGGTTGAT
GACGGTTGGGGTGAACGTCCGCTGtaaGAATT

B: BoNTA(H_c) encoded protein (Version #2) SEQ ID NO: 4

MSTFTEYIKNIINTSILNRYESNLIDLRSYASKINIGSKVNFDPIDKNQIQLF
NLESSKIEVILKNAIVYNSMYENFSTSFWRIPKYFNSISLNNEYTIINCMENNS
GWKVSLSNYGEIIWTLQDTQEIKQRVVFKYSQMINISDYNRWFVTITNNRLN
NSKIYINGRLIDQKPISNLGNIHASNIMFKLDGCRDTHRYWIKYFNLFDKE
LNEKEIKDLYDNQSNSGILKDFWGDYLQYDKPYYMLNYDPNKYVDVNNV
GIRGYMLKGPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRNNDRV
YINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSNDQGI
TNKCKMNLQDNNGNDIGFIGFHQFNNIAKLVASNWYNRQIERSRTLGCSW
EFPVDDGWGERPL*

FIGURE 3

A: BoNTA(H_c) synthetic gene (Version #3) SEQ ID NO: 5

GAATTCGAAACGatgGCCTCTACCTTCACTGAATAACATCAAGAACATCATC
AATAACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCT
GTCTCGCTACGCTTCCAAAATCAACATCGGCTCAAAGTTAACCTCGATC
CGATCGACAAGAACATCAGATCCAGCTGTCAATCTGAAATCTTCCAAAAT
CGAAGTTATCCTGAAGAACATGCTATCGTATAACAACCTATGTACGAAAAC
TCTCCACCTCCTCTGGATCCGTATCCGAAATACTTCAACTCCATCTCTC
TGAACAATGAATAACACCATCATCAACTGCATGGAAAACAATTCTGGTTG
GAAAGTATCTCTGAACTACGGTAAATCATCTGGACTCTGCAGGACACT
CAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGATCAACA
TCTCTGACTACATCAATCGCTGGATCTCGTTACCATCACCAACAATCGT
CTGAATAACTCCAAAATCTACATCAACCGCCGTCTGATCGACCAAGAAC
CGATCTCCAATCTGGTAACATCCACGCTCTAATAACATCATGTTCAA
CTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAA
TCTGTTGACAAAGAACTGAACGAAAAGAAATCAAAGACCTGTACGAC
AACCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGAACCTGCA
GTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATAC
GTTGACGTCAACAAATGTAGGTATCCGCGTTACATGTACCTGAAAGGTC
CGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACCTTCCCTGTAC
CGTGGTACCAAATTCTACATCAAGAAATACCGCTCTGGTAACAAGGACA
ATATCGTTGCAACAATGATCGTATACATCAATGTTGTTAGTAAGAAC
AAAGAATACCGTCTGGCTACCAATGCTCTCAGGCTGGTGTAGAAAAGA
TCTTGTCTGCTCTGGAAATCCGGACGGTGTAAATCTGTCTCAGGTAGTT
GTAATGAAATCCAAGAACGACCAAGGGTATCACTAACAAATGCAAATGA
ATCTGCAGGACAACAATGGTAACGATATCGGTTCATCGGTTCCACCAAG
TTCAACAATATCGCTAAACTGGTTGCTTCCAACGGTACAATCGTCAGAT
CGAACGTTCTCGCACTCTGGGGTGTCTGGGAGTTCATCCGGTTG
ATGACGGTTGGGGTGAACGTCCGCTGtaaGAATT

B: BoNTA(H_c) encoded protein (Version #3) SEQ ID NO: 6

MASTFTEYIKNIINTSILNLYESNLIDLSRYASKINIGSKVNFDPIDKNQIQL
FNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENN
SGWKVSLNYGEIIWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRL
NNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHR YIWIKYFNLFDK
ELNEKEIKDLYDNQSNNSGILKDFWGDYLQYDKPYYMLNL YDPNKYVDVNN
VGIRGYMYLKGPRGSVMTNTYLNSSLYRGTKFIKKYASGNKDNIVRNNDR
VYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSNDQ
GITNKCKMNLQDNNNGNDIGFIGFHQFNNIAKLVASNWYNRQIERSSRTLGC
WEFIPVDDGWGERPL*

FIGURE 4

A: BoNTB(H_c) synthetic gene SEQ ID NO: 7

GAATTCACGatgGCCAACAAATACAATTCCGAAATCCTGAACAATATCAT
CCTGAACCTGCGTACAAAGACAACAATCTGATCGATCTGTCGGTTACG
GTGCTAAAGTTGAAGTATAACGACGGTGTGAACCTGAATGACAAGAACCA
GTTCAAACGTGACCTCTCCGCTAACTCTAAGATCCGTTACTCAGAACATC
AGAACATCATCTCAACTCCGTATTCCCTGGACTCTCTGTTCCCTCTGGA
TTCGTATCCCGAAATACAAGAACGACGGTATCCAGAATTACATCCACAA
TGAATACACCATCATCAACTGCATGAAGAATAACTCTGGTTGGAAGATC
TCCATCCCGCGTAACCGTATCATCTGGACTCTGATCGATATCAACGGTAA
GACCAAATCTGTATTCTCGAATACAACATCCGTGAAGACATCTCTGAAT
ACATCAATCGCTGGTTCTCGTTACCATCACCAATAACCTGAACAATGCT
AAAATCTACATCAACGGTAAACTGGAATCTAATACCGACATCAAAGACA
TCCGTGAAGTTATCGCTAACGGTAAATCATCTCTCAAACCTGGACGGTGA
CATCGATCGTACCCAGTTACATCTGGATGAAATACTCTCCATCTCAACAA
CCGAACGTCTCAGTCCAATATCGAAGAACGGTACAAGAGATCCAGTCTTA
CTCCGAATACCTGAAAGACTCTGGGTAATCCGCTGATGTACAACAAA
GAATACTATATGTTCAATGCTGGTAACAAGAACTCTTACATCAAACCTGA
AGAAAGACTCTCCGGTTGGTAAATCCTGACTCGTCTCCAAATACAACCA
GAACTCTAAATACATCAACTACCGCGACCTGTACATCGGTGAAAAGTT
ATCATCCGTCGCAAATCTAACTCTCAGTCCATCAATGATGACATCGTACG
TAAAGAAGACTACATCTACCTGGACTTCTCAACCTGAATCAGGAATGG
CGTGTATACACCTACAAGTACTTCAAGAAAGAAGAAGAAAAGCTTTCC
TGGCTCCGATCTGATTCCGACGAACTCTACAACACCCTCAGATCAA
GAATACGACGAACAGCCGACCTACTCTGCCAGCTGCTGTTCAAGAAAG
ATGAAGAATCTACTGACGAAATCGGTCTGATCGGTATCCACCGTTCTAC
GAATCTGGTATCGTATTGAAAGAATACAAAGACTACTCTGCATCTCCAA
ATGGTACCTGAAGGAAGTAAACGAAACCGTACAACCTGAAACTGGGT
TGCAATTGGCAGTTCATCCGAAAGACGAAGGGTGGACCGAAtagtaaGAA
TTC

B: BoNTB(H_c) encoded protein SEQ ID NO: 8

MANKYNSEILNNIILNLRYKDNNNLIDLSGYGAKVEVYDGVELNDKNQFKLT
SSANSKIRVTQNQNIIFNSVFLDFSVSFWRIPKYKNDGIQNYIHNEYTIINCM
KNNSGWKISIRGNRIWTLIDINGKTKSVFFEYNIREDISEYINRWFFVTITNNL
NNAKIYINGKLESNTDIKDIREVIANGEIIFKLDGDIDRTQFTWMKYFSIFNTTEL
SQSNEIERYKIQSYSEYLKDFWGNPLMYNKEYYMFNAGNKNYSIKLKKDSP
VGEILTRSKYNQNSKYINYRDLYIGEKFIIRKNSQSINDDIVRKEDYIYLD
FNLNQEWRVYTYKYFKKEEKLFLAPISDSDELYNTIQIKEYDEQPTYSCQL
LFFKDEESTDEIGLIGIHRFYESGIVFEEYKDYFCISKWYLKEVKRKPYNLKL
GCNWQFIPKDEGWTE**

FIGURE 5

A: BoNTC₁(H_c) synthetic gene SEQ ID NO: 9

GAATTCACGatgACCATCCCATTCAACATCTTCTCCTACACCCAACAACCTCC
CTGTTGAAGGACATCATCAACGAGTACTTCACAAACATCAACGACTCCA
AGATCCTGTCCCTGCAGAACCGTAAGAACACACCTGGTCGACACCTCCGG
TTACAACGCCGAGGGTCTCCGAGGAGGGTGAACGTCCAGCTGAACCCAATC
TTCCCATTGACTTCAAGCTGGGTTCTCCCGGTGAGGACAGAGGTAAGGT
CATCGTCACCCAGAACGAGAACATCGTCTACAACTCCATGTACGAGTCC
TTCTCCATCTCCTCTGGATCAGAACATCAACAAGTGGGTCTCCAACCGCC
AGGITACACCATCATCGACTCCGTCAAGAACAACTCCGGTTGGTCCATCG
GTATCATCTCCAACCTCCTGGTCTCACCTGAAGCAGAACGAGGACTCC
GAGCAGTCCATCAACTCTCCTACGACATCTCAACAAACGCTCTGGTTA
CAACAAGTGGGTTCTCGTCACCGTACCAACAAACATGATGGGTAAACATG
AAGATCTACATCAACGGTAAGCTGATCGACACCATCAAGGTCAAGGAGT
TGACCGGTATCAACTCTCCAAGACCATCACCTCGAGATCAACAAGATC
CCAGACACCGGTCTGATCACCTCCACTCCGACAACATCAACATGTGGA
TCCGTGACTTCTACATCTCGCCAAGGAGTTGGACGGTAAGGACATCAA
CATCCTGTTCAACTCCTGCAGTACACCAACGTCGTAAGGACTACTGGG
GTAACGACCTGAGATAACAAACAGGAGTACTACATGGTCAACATCGACTA
CTTGAACAGATAACATGTACGCCAACTCCAGACAGATCGTCTCAACACC
AGACGTAACAAACAAACGACTTCAACGAGGGTTACAAGATCATCATCAAGC
GTATCAGAGGTAACACCAACGACACCCAGAGTCAGAGGTGGTACATCCT
GTACTTCGACATGACTATCAACAAACAGGCTTACAACCTGTTCATGAAG
AACGAGACCATGTACGCCACAACCAACTCCACCGAGGGACATCTACGCCA
TCGGTCTCGGTGAGCAGACCAAGGACATCAACGACAACATCATCTTCCA
GATCCAGCCAATGAACAAACACTTACTACTACGCTTCCCAGATCTTCAAGT
CCAACCTCAACGGTGAGAACATCTCCGGTATCTGTTCCATCGGTACCTAC
AGATTCCGTCGGGTGGTGAAGTGGTACAGACACAACACTTGGTTCCAAC
TGTCAAGCAGGGTAACACTACGCCCTTGCTGGAGTCCACTTCCACCCACT
GGGGATTCGTCCCAGTCTCCGAGtaatGAATTC

B: BoNTC₁(H_c) encoded protein SEQ ID NO: 10

MTIPFNIFSYTNNSSLKDIINEYFNNINDSKILSLQNRKNTLVDTSGYNAEVSE
EGDVQLNPFPDFKLGSSGEDRGKVVTQNEIVYNSMYESFSISFWIRINK
WVSNLPGYIIDSVKNNSGWSIGIISNFLVFTLKQNEDSEQSINFSYDISNNAP
GYNKWFFVTVTNNMMGNMKIYINGKLIDTIKVKELTGINSKTTFEINKPD
TGLITSDSDNINMWIRDFYIFAKELDGKDINILEFNSLQYTNVVKDYWGNDLR
YNKEYYMVNIDYLNRYMYANSRQIVFNRRNNNDFNEGYKIIKIRGNTN
DTRVRGGDILYFDMTINNKAYNLFMKNETMYADNHSTEDIYAILREQTKD
INDNIIIFQIOPMNNTYYASQIFKSNFNGENISGICSIGTYRFRLGGDWYRHIN
YLVPTVKQGNYASLLESTSTHWGFVPVSE**

FIGURE 6

A: BoNTD(H_c) synthetic gene SEQ ID NO: 11

GAATTCACGatcCGTTGAAGGCTAACGGTCAACGAGTCCCTCGAGAACAC
CATGCCATTCAACATCTTCTCCTACACCAACAACCTCCTGTTGAAGGACA
TCATCAACGAGTACTTCAACTCCATCAACGACTCCAAGATCTTGTCCCTG
CAGAACAAAGAACGCCCTGGTCGACACCTCCGGTACAACGCCGAGG
TCAGAGTCGGTGACAACGTCCAGTTGAACACCCTACACCAACGACTT
CAAGTTGTCCCTTCCGGTGACAAGATCATCGTCAACTTGAACAAACAACA
TCTTGTACTCCGCCATCTACGAGAACTCCTCTGTCTCCTCTGGATCAAG
ATCTCCAAGGACTTGACCAACTCCCACAACGAGTACACCCTACACTCAACT
CCATCGAGCAGAACTCCGGTTGGAAGTTGTATCCGTAACGGTAACCAT
CGAGTGGATCTGCAGGACGTCACCGTAAGTACAAGTCCCTGATCTTCG
ACTACTCCGAGTCCTGTCCCACACCGTTACACCAACAAAGTGGTTCTTC
GTCACCACATACCAACAACATCATGGGTTACATGAAGTTGTACATCAACG
GTGAGTTGAAGCAGTCCCAGAAGATCGAGGACCTGGACGAGGTCAAGCT
GGACAAGACCATCGTCITCGGTATCGACGAGAACATCGACGAGAACCAAG
ATGTTGTGGATCCGTGACTTCAACATCTTCTCCAAGGAGCTGTCCAACGA
GGACATCAACATCGTCTACGAGGGTCAGATCCTGAGGAACGTCATCAAG
GACTACTGGGTAACCCACTGAAGTTCGACACCGAGTACTACATCATCA
ACGACAACATCGACCGTTACATCGCCCCAGAGTCCAACGTCCTGGT
CCTGGTCCAGTACCCGTACCGTTCCAAGCTGTACACCGTAACCCCTATCA
CCATCAAGTCCGTCTCGACAAGAACCTTACTCCGTATCCTGAACGGT
GACAACATCATCCTGCACATGCTGTACAACCTCCGTAAGTACATGATCAT
CCGTGACACCGACACCATCTACGCCACCCAGGGTGGTGACTIONTCCCAG
AACTGTGTCTACGCCCTGAAGCTGCAGTCCAACCTGGGTAACTACGGTAT
CGGTATCTTCTCCATCAAGAACATCGTCTCCAAGAACAAAGTACTGCTCCC
AGATCTTCTCCTCCCTCCGTGAGAACACCATGCTGCTGGCCGACATCTAC
AAGCCTGGCGTTCTCCTCAAGAACGCCAACACTCCTGTCGCCGTAC
CAACTACGAGACCAAGCTGCTGTCACCTCCTCCTCTGGAAAGTTCATCT
CCCGTACCCAGGGTGGTCGAAGatAGGAATT

B: BoNTD(H_c) encoded protein SEQ ID NO: 12

MRLKAKVNESFENTMPFNIFSYTNNSLKDIINEYFNSINDSKILSLQNKNA
LVDTSGYNAEVRVGDNVQLNTIYTNDFKLSSSGDKIVNLNNNLYSAIYENS
SVSFWikISKDLTNSHNEYTIINSIEQNSGWKLCIRNGNIEWILQDVNRKYKS
LIFDYESLSSHTGYTNKWFFVTITNNIMGYMKLYINGELKQSQKIEDLDEVK
LDKTIVFGIDENIDENQMLWIRDFNIFSKELSNDINIVYEGQILRNVIKDYW
GNPLKFDTTEYYIINDNYIDRYIAPESNVLVLVQYPDRSKLYTGNPITIKSVSD
KNPYSRILNGDNIILHMLYNSRKYMIIRDTDIYATQGGDCSQNCVYALKLQ
SNLGNYGIGIFSNIKVNKNYCSQIFSSFRENTMLLADIYKPWRFSFKNAYT
VAVTNYETKLLSTSSFWKFISRDPGWVE**

FIGURE 7

A: BoNTE(H_c) synthetic gene SEQ ID NO: 13

GAATTCAACatgGGAGAGAGTCAGCAAGAACTAAATTCTATGGTAACGTAA
TACCCCTAAATAATAGTATTCTTAAAGCTTCTTCTTACAGATGATAA
AATTAAATTCTACTTCAACAAGTCTCAAGAGAATTAAGTCTTCTC
CGTTAAACATGAGATACAAGAATGATAAATACGTCGACACTCCGGT
TACGACTCCAATATCAACATTAACGGTGACGTGTACAAGTACCCAACTA
ACAAAAACCAATTGGTATCTACAACGACAAGCTTACTGAGCTGAACAT
CTCTAAAACGACTACATTCTACGACAACAAGTACAAGAACTTCTCTA
TTTCTTCTGGTCAGGATTCTAACTACGACAACAAGATCGTCAACGTT
AACAAACGAGTACACTATCATCAACTGTATGAGAGACAACAACCTCCGGT
GGAAGGTCTCTCTAACCAACGAGATCATTGGACCTTGCAGACAA
CGCAGGTATTAACCAAAAGTTAGCATTCAACTACGGTAACGCAAACGGT
ATTCTGACTACATCAACAAGTGGATTTCTCACTATCACTAACGACAG
ATTAGGTGACTCTAACGTTACATTACGGTAACTTAATCGACCAAAAGT
CCATTAAACTTAGGTAACATTACGTTCTGACAAACATCTTATTCAAG
ATCGTTAACTGCAGTTACACCAGATACTGGCATTAGATACTTCAACAT
TTTCGACAAGGAGTTAGACGAGACCGAGATTCAAACCTTATACAGCAAC
GAACCTAACACCAATATTGAGGACTTCTGGGTAACTACTTGCTTTA
CGACAAGGAATACTACTTATTAAACGTGTTAAAGCCAAACAACCTCATT
GATAGGAGAAAGGATTCTACTTAAACGCTTAAGCATTAAACAACATCAGAAGCAGT
TTCTTCTAGCTAACAGATTATACTCTGGTATCAAGGTTAAAGATCCAAAGA
GTTAACAACTCTTACTAACGATAACCTGTTAGAAAGAACGATCAGGT
CTATATTAACCTCGCTAGCAAGACTCACTTATTCCCATTATATGCTG
ATACCGCTACCAACAAAGGAGAAAGACCATCAAGATCTCCTCTGG
CAACAGATTAAACCAAGTCGCTGTTATGAACCTCGTCGGTAACAACTGTA
CCATGAACTTAAAAATAATAATGGAAATAATATTGGGTTTAGGTTTC
AAGGCAGATACTGTAGTTGCTAGTACTGGTATTATACCCACATGAGAG
ATCACACCAACAGCAATGGATGTTTGGAACTTATTCTGAAGAACAT
GGATGGCAAGAAAAAtaa
TagGGATCC GCGGCCGC ACGCGT CCCGGG ACTAGT GAATT

B: BoNTE(H_c) encoded protein SEQ ID NO: 14

MGESQQELNSMVTDTLNNSIPFKLSSYTDDKILISYFNKFFKRIKSSSVLNMR
YKNDKYVDTSGYDSNININGDVYKYPNKNQFGIYNDKLTELNISQNDYIY
DNKYKNFSISFWVRIPNYDNKIVNVNNEYTIINCMRDNNSGWKVSLNHNEII
WTLQDNAGINQKLAFLNYGNANGISDYINKWIFVTITNDRLGDSKLYINGNLI
DQKSILNLGNIHVDNILFKIVNCSYTRYIGIRYFNIFDKELDETEIQTLYSNEP
NTNLIKDFWGNYLLYDKEYYLLNVLKPNNFIDRRKDSTLSINNIRSTILLANR
LYSGIKVKIQRVNNSTNDNLVRKNDQVYINFVASKTHLFPLYADTATTNKE
KTIKISSSGNRFNQVVVMNSVGNNCTMFKNNNNGNNIGLLGFKADTVVAST
WYYTHMRDHTNSNGCFWNFISEEHGWQEK**

Endorsement 1

DESIGNED NUCLEOTIDE SEQUENCE OF BONTE(Hc)

FIGURE 9

A: BoNTF(H_c) synthetic gene SEQ ID NO: 15

GAATTCACGatgTCCTACACCAACGACAAGATCCTGATCTGTACTTCAAC
AAGCTGTACAAGAAGATCAAGGACAACCTCCATCTTGGACATGAGATAACG
AAAACAATAAGTCATCGACATCTCCGGTTACGGTTCCAACATCTCCATC
AACGGTGACGTCTACATCTACTCCACCAATAGAAACCAAGTTCGGAATCT
ACTCCTCCAAGCCTCCGAGGTCAACATCGCTCAGAACAAACGACATCAT
CTACAACGGAAGATAACCAGAACCTCTCCATCTCCTCTGGGTCCGTATCC
CAAAGTACTTCAACAAAGGTCAACCTGAATAACGAGTACACCATCATCGA
CTGCATCCGTAAACAATAACTCCGGATGGAAGATCTCCCTGAACACTAACAC
AAGATCATCTGGACCCCTGCAGGACACCGCCGGTAACAATCAGAAGTTGG
TCTTCAACTACACCCAGATGATCTCCATCTCCGACTACATCAACAAGTGG
ATCTTCGTACCATACCAATAACCGTTGGAAACTCCAGAACATCTACAT
CAACGGTAACCTGATCGACGAGAAGTCCATCTCCAACCTGGGTGACATC
CACGTCTCCGACAACATTGTTCAAGATCGTCGGTTGTAACGACACCCG
TTACGTGGGATCCGTTACTTCAAAGTCTCGACACTGAGTTGGTAAGA
CCGAGATCGAGACCTGTACTCCGACGAGCCTGACCCATCCATCCTGAA
GGACTTCTGGGTAACTACCTGCTGTACAACAAACGTTACTACTGCTGA
ACTTGTGCGTACCGACAAGTCCATACCCAGAACCTCCAACTTCTGAAAC
ATCAACCAGCAGAGAGGTGTCTACCGAGAACGCCAAACATCTCTCCAACA
CCAGATTGTACACCGGAGTCGAGGTATTACAGAAAGAACGGATCTAC
TGATATTCCAACACCGATAACTTCGTCAAGAAAGAACGATCTGGCTTACA
TCAACGTTGTCGACAGAGATGTCGAATACCGTCTGTACGCCGATATCTCT
ATCGCCAAACCTGAAAAGATCATCAAGCTGATCCGTACCTCTAACTCTA
ACAACCTCTGGGACAACATCGTCATGGACTCCATCGGTAAATAACTGT
ACCATGAACCTCCAGAACACAACGGTGGAAACATCGGTTGTTGGGTT
TCCACTCCAACAACCTGGTCGCTCCTCCTGGTACTACAACAAACATCCGT
AAGAACACCCCTCCAACGGTTGCTCTGGCTTCACTCCAAGGAGCA
CGGTTGGCAGGAGAACtaatagGAATT

B: BoNTF(H_c) encoded protein SEQ ID NO: 16

MSYTNDKILLYFNKLKYKKIKDNSILDMDRYENNKFIDISGYGSNISINGDVYIY
STNRNQFGIYSSKPSEVNIAQNNDIIYNGRYQNFSISFWVRIPKYFNKVNLLNN
EYTIIDCIRNNNSGWKISLNLYNKKIWTLQDTAGNNQKLVFNYTQMISISDYIN
KWIFVTITNNRLGNSRJYINGNLIDEKSIISNLGDIHVSNDLFLKIVGCNDTRYV
GIRYFKVFDTELGKTEIETLYSDEPDPSILKDFWGNYLLYNKRYYYLLNLLRT
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIILKIRTSNSNNSLGQIIVMDSI
GNNTMNFQNNNGGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS
KEHGWQEN**

FIGURE 10

A: BoNTG(H_c) synthetic gene SEQ ID NO: 17

GAATTCACGatgAAGGACACCACCTGATCCAGGTCTTCAACAACTACATC
TCCAACATCTCCTCCAACGCCATCCTGTCCTTACCGTGGTGGTCG
TCTGATCGACTCCTCCGGTTACGGAGCCACCATGAACGTCGGTCCGACG
TCATCTTCAACGACATCGGTAACGGTCAGTTCAAGCTGAACAACTCCGA
GAACCTCCAACATCACCAGCCCACCACTCCAAGTTCGTCGTCTACGACTCCA
TGTCGACAACATTCTCCATCAACTCTGGGTCCGTACCCAAAGTACAAC
AACAAACGACATCCAGACCTACCTGCAGAACGAGTACACCATCATCTCCT
GTATCAAGAACGACTCCGGTTGGAAAGGTCTCCATCAAGGGAAACCGTAT
CATCTGGACCCCTGATCGACGTCACGCCAACGTCACGTTCTTCG
AGTACTCCATCAAGGACAACATCTCCGACTACATCAACAAGTGGTCTCC
ATCACCATCACCAACGACCGTCTGGTAACGCCAACATCTACATCAACG
GTTCCCTGAAGAAGTCCGAGAAGATCTGAACCTGGACCGTATCAACTC
CTCCAACGACATCGACTTCAAGCTGATCAACTGTACCGACACCCACCAAG
TTCGTCTGGATCAAGGACTTCAACATCTCGTGTGAGCTGAACGCCAC
CGAGGTCTCCCTGTACTGGATCCAGTCCTCCACCAACACCCCTGAAGG
ACTTCTGGGAAACCCACTGCGTTACGACACCCAGTACTACCTGTTCAAC
CAGGGTATGCGAGAACATCTACATCAAGTACTTCTCAAGGCTCCATGG
GTGAGACCGCCCCCTCGTACCAACTTCAACAAACGCCACATCAACTACCA
GAACCTGTACCTGGGTCTGCGTTCATCATCAAGAAGGCTCCAACCTCCC
GTAACATCAACAACGACAACATCGTCCGTGAGGGTGACTACATCTACCT
GAACATCGACAACATCTCCGACGAGTCTACCGTGTACGTCTGGTCA
ACTCCAAGGAGATCCAGACCCAGCTGTTCTGGCCCCAATCAACGACGA
CCCTACCTTCTACGACGTCTGCGATCAAGAAGTACTACGAGAACGACC
ACCTACAACGTGACGATCTGTGCGAGAAGGACACCAAGACCTCGGAC
TGTCGGTATCGGTAGTCTGCAAGGACTACGGTTACGTCTGGACACC
TACGACAACACTTCTGTATCTCCAGTGGTACCTGCGTGTATCTCCGA
GAACATCAACAAGCTCGTCTGGATGTAACGGCAGTTCATCCCAGTC
GACGAGGGTTGGACCGAGtaatAGAATTC

B: BoNTG(H_c) encoded protein SEQ ID NO: 18

MKDTILIQVFNNYISNISSNAILSLSYRGGRLLIDSSGYGATMNVGSDVIFNDIG
NGQFKLNNSENSNITAHQSKFVYDSMFDNFNSINFWV RTPKYN>NNNDIQTYL
QNEYTIISCIKNDSGWKVSIKGRIIWTLLDVNAKSKSIFFEYSIKDNISDYINK
WFSITITNDRLGNANIYINGSLKKSEKILNLDRINSSNDIFKLINCTDTKFV
WIKDFNIFGRELNATEVSSLWYIQSSTNTLKDFWGNPLRYDTQYYLFNQGM
QNIYIKYFSKASMGETAPRTNFNNAAINYQNLYLGLRFIKKASNSRNINNDN
IVREGDYIYLNIDNISDESYRVYVLVNSKEIQTQLFLAPINDDPTFYDVLQIKK
YYEKTTYNCQILCEKDTKTFGLFGIGKFVKDYGYVWDTYDNYFCISQWYLR
RISENINKRLGCNWQFIPVDEGWTE**

FIGURE 11

A: BoNTA(H_n) synthetic gene SEQ ID NO: 19

atgGCTCTGAACGACCTGTGCATCAAAGTTAACAACTGGGACCTGTTCTCTCCCGTCTGAAGACAACTTCACTAACGACCTGAACAAAGGCGAAGAAA
TCACCTCCGACACTAACATCGAAGCTGCTGAAGAAAACATCTCTCTGGACCTGATCCAGCAGTACTACCTGACTTCAACTTCGACAACGAACCGGAA
AACATCTCCATCGAAAACCTGTCTTCCGACATCATCGGTCAAGCTGGAACTGATGCCAACATCGAACCGCTCCGAACGGCAAGAAATACGAACGGAC
AAATACACCATGTTCCACTACCTGCGTGCAGGAATTGAACACACGGTAATCTCGTATCGCTCTGACTAACCGTTAACGAAGCTCTGCTGAACCCG
TCTCGCGTTACACCTCTTCTCCGACTACGTTAACGAAAGTTAACAAAGCTACTGAAGCTGCTATGTTCCCTGGGTTGGGTTGAACAGCTGGTTACG
ACTTCACCGACGAAACTCTGAAGTTCCACCACTGACAAAATCGCTGACATCAGTACATCGGTAAACATCGCTGACATCACTATCATCCC
GCTGTACAAAGACGACTTCGTTGGCTCTGATCTCTGGCTGTTCCTGGGTTACCTTCGCTGGGTTCTGGGTTACCTTCGCTGGTTACCTTC
GCTCTGGTTTCCTACATCGCTAACAAAGTTCTGACTGTTCAAGGACCATCGAACCGCTGTCTAACGCTGTCTAACGAAAGTTAACAAATAC
ATCGTTACTAATGGCTGGCTAAAGTTAACACTCAGATCGACCTGATCCGTAAGAAGATGAAAGAAGCTCTGGAAAACCAGGCTGAAGCTACTAAAGC
TATCATCAACTACCAAGTACAACCAACAGTACACCGAAGAAGAAAAGAACAAACATCAACTTCAACATCGATGACCTGCTCTAAACTGAACGAATCC
CAAAGCTATGATCAACATCAACAAATTCTGAACCGAGTCTGTTCTGGGCTGTCTGGGTTACCTTCGCTGGGTTACCTTCGCTGGGTTACCTTC
ACCTGATGAACTCTATGATCCGTACGGCGTTAACCGCCTGGAAAGACTTCGACGCTTCCCTGAAAGACGCTCTGCTGAAATACATCCGTAACACTACG
GTACTCTGATGGCCAGGTTGACCGTCTGAAAGACAAGGTTAACAAACACCTGTCTACTGACATCCGTTCCAGCTGTCCAAATACGTTGACAACCAAG
a

B: BoNTA(H_n) encoded protein SEQ ID NO: 20

MALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEITSDTNIEAAEENISLDLIQ
QYYLTNFNDNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHY
LRAQEFEHGKSRIALTNVNEALLNPSRVYTFFSDYVKKVNKATEAAMFL
GWVEQLVYDFTDETSEVSTTDKIADITIIIPYIGPALNIGNMLYKDDFVGALIF
SGAVILLEFIPEIAIPVLTGTFALVSYIANKVLTQTDNALSKRNEKWDEVYK
YIVTNWLAKVNTQIDLIRKKMKEALENQAEATKAIINYQYNQYTEEKNNI
NPNIDDLSSKLNESINKAMININKFLNQCSVSYLMNSMIPYGVKLEDFDASL
KDALLKYIRDNYGTLIGQVDRLKDKVNNTLSTDIPFQLSKYVDNQ*

FIGURE 12

A: BoNTB(H_n) synthetic gene SEQ ID NO: 21

atgGCTCCAGGAATCTGTATCGACGTGACAACGAGGACTTGTCTTCATC
GCTGACAAGAACTCCTCTCCGACGACTTGTCCAAGAACGAGAGAACG
AGTACAACACCCAGTCCAACATACATCGAGAACGACTTCCAATCAACGA
GTTGATCTTGGACACCGACTTGATCTCCAAGATCGAGTTGCCATCCGAGA
ACACCGAGTCCTTGACTGACTCAACGTCACGTCCCAGTCTACGAGAA
GCAACCAGCTATCAAGAAGATTTCACCGACGAGAACACCATCTTCAA
TACCTGTACTCTCAGACCTCCCTTGGACATCAGAGACATCTCCTTGAC
CTCTCCTCGACGACGCCCTGCTGTTCTCCAACAAGGTCTACTCCTTCTT
CTCCATGGACTACATCAAGACTGCTAACAAAGGTGTCGAGGCCGGTTG
TTCGCTGGTTGGGTCAAGCAGATCGTCAACGATTGTCATCGAGGCTAA
CAAGTCCAACACCATGGACAAGATTGCCGACATCTCTGATTGTCCCAT
ACATCGGTTGGCCTGAAACGTCGCTAACGAGACGCCAAGGGTAACCT
CGAGAACGCTTCGAGATCGTGGTGCCTCCATCTGTTGGAGTTCATCC
CAGAGTTGTTGATCCCAGTCGTCGGTGCCTTCTGTTGGAGTCTACATC
GACAACAAGAACAGATCATCAAGACCATCGACAACGCTTGACCAAGA
GAAACGAGAACGGTCCGACATGTACGGTTGATCGTCGCCAATGGTT
GTCCACCGTCAACACCCAATTCTACACCATCAAGGAGGGTATGTACAAG
GCCTGAACTACCAAGGCCAAGCTTGGAGGAGATCATCAAGTACAGAT
ACAACATCTACTCCGAGAACGGAGAACGACTTCAAACATCGACTTCAA
CGACATCAACTCCAAGCTGAACGAGGGTATTAAACAGGCCATCGACAAC
ATCAACAACITCATCAACGGTTGTTCCGTCTCCTACTTGATGAAGAACG
GATTCCATTGGCCGTCGAGAACGTTGGACTTCGACAACACCCCTGAAG
AAGAACATTGTTGAACATCGACGAGAACAGTTGACTTGATCGGTT
CCGCTGAGTACGAGAACGTCAGAGTCAACAAAGTACTTGATGAAGACCATCAT
GCCATTGACTTGTCCATCTACACCAACGACACCATTGATCGAGATGT
TCtaa

B: BoNTB(H_n) encoded protein SEQ ID NO: 22

MAPGICIDVDNEDLFFIADKNSFSDDLSKNERIEYNTQSNYIENDFPINELILD
TDLISKIELPSENTESLTDFNVDVPVYEKQPAIKKIFTDENTIFQYLYSQTFPLD
IRDISLTSSFDDALLFSNKVYSFFSMDYIKTANKVVEAGLFAGWVKQIVNDF
VIEANKSNTMDKIADISLIVPYIGLALNVGNETAKGNFENAFEIAGASILLEFI
PELLIPVVGAFLLESYIDNKNKIKTIDNALTKRNEKWSDMYGLIVAQWLST
VNTQFYTIKEGMYKALNYQAQALEEIIK YR YNIYSEKEKSNIIDFNDINSKL
NEGINQAIIDNINNFINGCSVSYLMKKMPLAVEKLLFDNTLKKNLLNYIDE
NKLYLIGSAEYEKSKVNKYLKTIIMPFDLSIYTNDTILIEMF*

FIGURE 13

A: BoNTC₁(H_N) synthetic gene SEQ ID NO: 23

atgTCCCTGTACAACAAGACCCTGACTGTAGAGAGCTGCTGGTGAAGAA
CACTGACCTGCCATTCATCGGTGACATCAGTGACGTGAAGACTGACATCT
TCCTGCGTAAGGACATCAACGAGGAGACTGAGGTGATCTACTACCCAGA
CAACGTGTCAGTAGACCAAGTGATCCTCAGTAAGAACACCTCCGAGCAT
GGACAACTAGACCTGCTCACCTAGTATCGACAGTGAGAGTGAGATCC
TGCCAGGGGAGAATCAAGTCTTACGACAACCGTACCCAGAACGTGGA
CTACCTGAACCTCCTACTACTACCTAGAGTCTCAGAACGACTGAGTGACAAC
GTGGAGGACTTCACTTACCGCGTCAATCGAGGAGGCTCTGGACAACA
GTGCAAAGGTGTACACTTACTTCCCTACCCCTGGCTAACAAAGGTGAATGCC
GGTGTGCAAGGTGGTCTGTTCTGATGTGGGCAAACGACGTGGTTGAGG
ACTTCACTACCAACATCCTGCGTAAGGACACACTGGACAAGATCTCAGA
TGTGTCAGCTATCATCCCTACATCGGACCCGCACTGAACATCTCCAAC
CTGTGCGTCGTGAAACTTCACTGAGGCATTGCACTGGTGTCA
ATCCTGCTGGAGGCATTCCCTGAGTTACAAATCCCTGCTCTGGGTGCATT
CGTGATCTACAGTAAGGTCCAGGAGCGAAACGAGATCATCAAGACCATC
GACAACGTCTGGAGCAGAGGATCAAGAGATGGAAGGACTCCTACGAGT
GGATGATGGGAACGTGGTTGTCAGGATCATCACCCAGTTAACAAACAT
CTCCTACCAGATGTACGACTCCCTGAACTACCAGGCAGGTGCAATCAAG
GCTAAGATCGACCTGGAGTACAAGAAGTACTCCGGAAGCGACAAGGAG
AACATCAAGAGGCCAGGTGAGAACCTGAAGAACAGTCTGGACGTCAAG
ATCTCGGAGGCATGAACAAACATCAACAAGTTCATCCGAGAGTGCTCCG
TCACCTACCTGTTCAAGAACATGCTGCCATTAGGTGATCAACCTGATCGACTCC
CATAACATCATCCTGGTCGGTGAGGTCGACAAGCTGAAGGCAAAGGTAA
ACAACAGCTTCCAGAACtaa

B: BoNTC₁(H_N) encoded protein SEQ ID NO: 24

MSLYNKTLDCRELLVKNTDLPFIGDISDVKTDIFLRKDINEETEVYYPDNVS
VDQVILSKNTSEHGQLDLLYPSIDSESEIIPGENQVFYDNRTQNVDYLN
YLESQKLSDNVEDFTFTRSIEEALDNSAKVYTYFPTLANKVNAGVQGGLFL
MWANDVVEDFTTNILRKDTLDKISDVSAIIPYIGPALNISNSVRRGNFTEAFA
VTGVILLEAFPEFTIPALGAFVIYSKVQERNEIIKTTIDNCLEQR
WMMGTWLSRIITQFNISYQMYDSLNYQAGAIKAKIDLEYKKYSGSDKENI
KSQVENLKNNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNEFDRN
TKAKLINLIDSHNIILVGEVDKLKAKVNNSFQN*

FIGURE 14

A: BoNTD(H_N) synthetic gene SEQ ID NO: 25

atggccAACTCCCGTGACGACTCCACCTGCATCAAGGTCAAGAACAAACAGA
CTGCCATACGTTGCCGACAAGGACTCCATCTCCAGGAGATCTTCGAGA
ACAAGATCATCACCAGACGAGACCAACGTTCAAAACTACTCCGACAAGTT
CTCTTGACGAGTCCATCCTGGACGGTCAGGTCCCAATCAACCCAGAG
ATCGTCGACCCACTGTTGCCAACGTCAACATGGAGCCATTGAAC TGCC
AGGTGAGGAGATCGTCTTCTACGACGACATCACCAGTACGTGACTAC
TTGAACCTCTACTACTACTTGAGTCTCAAAAGTTGTCTAACAAACGTCGA
GAACATCACCTGACCACCTCCGTGAGGAGGGCTTGGGTTACTCTAAC
AGATCTACACCTCCTGCCATCCTGGCTGAGAAGGTTAACAAAGGGTGT
CAAGCTGGTTGTTCTGAACTGGCCAACGAGGTGTCGAGGACTTCA
CCACCAACATCATGAAGAAGGACACCCCTGGACAAGATCTCGACGTCTC
CGTCATCATCCCATACTCGGTCCAGCCTTGAAACATCGGTAACTCCGCC
TGAGAGGTAACCTCAACCAGGCCTTCGCCACCGCCGGTGTGCGCCTCCTG
CTGGAGGGTTTCCAGAGTTACCATCCCAGCCCTGGGTGTCTCACCTT
CTACTCCTCCATCCAGGAGAGAGAGAAGATCATCAAGACCATCGAGAAC
TGCTTGGAGCAGAGACTAAGAGATGGAAGGACTCCTACCAAGTGGATGG
TTTCCAACGGCTGTCCAGAACATACCACCCAATTCAACCACATCAACTAC
CAGATGTACGACTCCCTGTCCTACCAAGGCCAGGCCATCAAGGCCAAGA
TCGACCTGGAGTACAAGAAGTACTCCGGTCCGACAAGGAGAACATCAA
GTCCCAGGTGAGAACCTGAAGAACTCCTGGACGTCAAGATCTCGAG
GCCATGAACAAACATCAACAAAGTACATCCGTGAGTGTCCGTACACCT
GTTCAAGAACATGCTGCCAAAGGTACGAGCTGAACAAGTTGAC
CTGAGAACCAAGACCGAGCTGATCAACCTGATCGACTCCACAAACATCA
TCCTGGTTGGTGAGGTTGACTaa

B: BoNTD(H_N) encoded protein SEQ ID NO: 26

MANSRDDSTCIKVKNRRLPYVADKDSISQEIFENKIJTDETNVQNYSDKFSLD
ESILDGQVPINPEIVDPLLPNVNMEPLNLPGEIIVFYDDITKYVDYLNSYYL
ESQKLSNNVENITLTTVEEALGYSNKIYTFPLPSLAEKVNKGVQAGLFLNWA
NEVVEDFTTNIMKKDTLDKISDVSIIPYIGPALNIGNSALRGNFNQAFATAG
VAFLLEGFPEFTIPALGVFTFYSSIQEREKIIKTIENCLEQRVKRWKDSYQWM
VSNWLSRITTQFNHINYQMYDSLSYQADAIAKAKIDLEYKKYSGSDKENIKSQ
VENLKNSLDVKISEAMNNINKFIRECSVTLFKNMLPKVIDELNKFDLRTKT
ELINLIDSHNIIIVGEVD*

FIGURE 15

A: BoNTE(H_n) synthetic gene SEQ ID NO: 27

```
atgTCCATCTGCATCGAGATCAACAACGGTGAGCTGTTCTCGTGGCTTCC  
GAGAACAGTTACAACGATGACAACATCAACACTCCTAAGGAGATTGACG  
ACACCGTCACCTCTAACAAACAACACTACGAAAACGACCTGGACCAGGTCA  
CCTAAACTTCAACTCCGAGTCCGCCCTGGTCTGTCCGACGAGAAGCTGA  
ACCTGACCATCCAGAACGACGCTTACATCCAAAGTACGACTCCAACGG  
TACATCCGATATCGAGCAGCATGACGTTAACGAGCTAACGTCTTCTTCT  
ACTTAGACGCTCAGAAGGTGCCGAGGGTGAGAACAAACGTCAATCTCAC  
CTCTCAATTGACACAGCCTGTTGGAGCAGCCTAACGATCTACACCTCT  
TCTCCTCCGAGTTCATCAACAACGTCAACAAGCCTGTGCAGGCCGCATTG  
TTCGTAAGCTGGATTCACTCAGCAGGTGTTAGTAGACTCACTACTGAGGCTAA  
CCAGAAGTCCACTGTTGACAAGATCGCTGACATCTCATCGTCGCCAT  
ACATCGGTCTGGCTCTGAACATCGGCAACGAGGCACAGAACAGGGCAACTT  
CAAGGATGCCCTGAGTTGGTGGCGGTATTTGTTGGAGTTCGAAC  
CCGAGCTGCTGATCCCTACCATCCTGGTCTCACGATCAAGTCCTCCTG  
GGTCCTCCGACAACAAGAACAGGTCAATTAGGCCATCAACAAACGCC  
TGAAGGAGCGTGACCGAGAACAGTGGAGGAAGTCTATTCCCTCATCGTCTC  
GAACCTGGATGACCAAGATCAACACCCAGTTCAACAAGCGAAAGGAGCA  
GATGTACCAGGCTCTGCAGAACCCAGGTCAACGCCATCAAGACCATCATC  
GAGTCCAAGTACAACCTCCTACACCCTGGAGGAGAACGAGCTTACCA  
ACAAGTACGATATCAAGCAGATCGAGAACGAGCTGAACCAGAACGGTCTC  
CATGCCATGAACAAACATCGACAGGTTCTGACCGAGTCCTCCATCTCCT  
ACCTGATGAAGCTCATCAACGAGGTCAAGATCAACAAAGCTGCGAGAGTA  
CGACGAGAAATGTCAAGACGTACCTGCTGAACATCATCCAGCACCGGA  
TCCATCCTGtaa
```

B: BoNTE(H_n) encoded protein SEQ ID NO: 28

```
MSICIEINNGELFFVASENSYNDNINTPKEIDDVTTSNNNYENDLDQVILNF  
NSE SAPGLSDEKLNLTIQNDAYIPKYDSNGTS DIEQHDVNELVFFYLD  
AQK VPEGENVNLTSSIDTALLEQP KIYTFFFSEFINNVNKP  
VQAALFVSWIQQVL  
VDFTTEANQKSTVDKIADISIVPYIGLALNIGNEAQKG  
NFKDALELLGAGIL  
LEFEPELIPTILVFTIKSFLGSSDNKNKVIKAINNALKERDEK  
WKEVYSFIVS  
NWMTKINTQFNKRKEQMYQALQNQVNAIKTIESK  
YNSYTLEEKNELTNKY  
DIKQIENELNQKVSIAMNNIDRFLTESSIS YLMKLINEVK  
INKLREYDENVKT  
YLLNYIIQHGSIL*
```

FIGURE 16

A: BoNTF(H_n) synthetic gene SEQ ID NO: 29

atgGCCCCACCAACGCTGTATTAGAGTCACAACTCAGAATTATTCTT
GTCGCTTCCGAGTCAAGCTACAACGAGAACGATATTAACACACCTAAAG
AGATTGACGATACTACCAACCTAAACAACAACCTACCGGAACAACCTGGA
TGAGGTTATTTGGATTACAACCTCACAGACCATCCCTCAAATTCCAACC
GTACCTAAACACTCTGTCCAAGACAACCTCCTACGTTCCAAGATAACGAT
TCTAACGGTACCTCAGAGATCGAGGAGTATGATGTTGACTTAAACGT
CTTTTCTATTGCATGCCAGAAGGTGCCAGAAGGTGAAACCAACATCT
CATTGACTCTCCATTGATACCGCCTGTTGGAAGAGTCAAGGATATC
TTCTTTCTCGGAGTTATCGATACTATCAACAAGCCTGTCAACGCCGC
TCTGTTATTGATTGGATTAGCAAGGTATCAGAGATTACCACTGAAG
CTACTCAAAGTCCACTGTTGATAAGATTGCTGACATCTCTTGATTGTC
CCCTATGTCGGTCTTGCTTGAACATCATTATTGAGGCAGAAAAGGGTAA
CTTGAGGAGGCTTTGAATTGTTGGAGTTGGTATTTGTTGGAGTTG
TTCCAGAACTTACCAATTCTGTCAATTAGTTTACGATCAAGTCCTACA
TCGATTACGAGAACAAAGAATAAAGCAATTAAAGCTATTAAACAAC
CTTGATCGAAAGAGAGGCTAAGTGGAAAGGAATCTACTCATGGATTGTA
TCAAACGGCTACTAGAATTAAACACTCAATTAAACAAGAGAAAGGAGC
AAATGTACCAGGCTCTGCAAAACCAAGTCGATGCTATCAAGACTGCAAT
TGAATACAAGTACAACAACACTATACTTCCGATGAGAAGAACAGACTGAA
TCTGAATACAATATCAACAAACATTGAAGAAGAGTTGAACAAGAAAGTT
CTTGCTATGAAGAATATCGAAAGATTATGACCAGATCCTCTATCT
TACTGATGAAGTTGATCAATGAGGCCAAGGGTGGTAAGTTGAAGAAGT
ACGATAACCACGTTAAGAGCGATCTGCTGAACATCTCGACCACAG
ATCAATCCTGGAGAGCAGACAAACGAGCTGAGTGAATTGGTTACTTCC
ACTTGAACTCCTCCATTCCATTGAGCTTCTaa

B: BoNTF(H_n) encoded protein SEQ ID NO: 30

MAPPRLCIRVNNSEFFVASESSYNENDINTPKEIDDNNLNNNNYRNNLDEVI
LDYNSQTIPQISRTLNTLVQDNSYVPRYDSNGTSEIEYDVDFNVFFYLH
AQKVPEGETNISLTSSIDTALLESKDIFSSSEFIDTINKPVNAALFIDWISKVIR
DFTTEATQKSTVDKIADISLIVPYVGLALNIIIIEAKGNFEEAFELLGVGILLEF
VPELTIPVILVFTIKSYIDSYENKNKAIAKAINNSLIEREAKWKEIYSWIVSNWL
TRINTQFNKRKEQMYQALQNVDAIKTAIEYKYNNTSDEKNRLESEYNIN
NIEEELNKKVSLAMKNIERFMTTESSISYLMKLINEAKVGKLKYDNHVKS
LNYILDHRSILGEQTNELSDLVTSTLNSSIPFELS*

FIGURE 17

A: BoNTG(H_n) synthetic gene SEQ ID NO: 31

atggccAAAAATACCGTAAATCTGAACAGTGTATTATTGTTAATAATGAG
GATTATTTCTAGCTAATAAAGATAGTTTCAAAAGATTAGCTAA
AGCAGAAACTATAGCATATAATACACAAAATAACTATAGAAAATAAT
TTTCTATAGATCAGTGATTAGATAATGATTAAAGCAGTGGCATAGA
CTTACCAAATGAAAACACAGAACCAATTACAAATTGACGACATAGAT
ATCCCTGTGTATATTAAACAATCTGCTTAAAAAAATTGTGGATGG
AGATAGCCTTTGAATATTACATGCTAAACATTCCCTCTAATATAG
AAAATCTACAACTAACGAATTCACTAAATGATGCTTAAAGAAATAATAA
TAAAGTCTACTTTCTACAAACCTTGTGAAAAAGCTAATACAG
TTGTAGGTGCTTCACTTTGAAACTGGTAAAAGGAGTAATAGATGAT
TTTACATCTGAATCCACACAAAAAGTACTATAGATAAAGTTCAGATGT
ATCCATAATTATCCCTATATAGGACCTGCTTGAATGTAGGAAATGAAA
CAGCTAAAGAAAATTAAAGCTTGTGAAATAGGTGGAGCCGCTAT
CTTAATGGAGTTATTCCAGAACTTATTGTACCTATAGTTGGATTITAC
ATTAGAACATATGTAGGAAATAAGGGCATATTATTGACGATATCC
AATGCTTAAAGAAAAGGGATCAAAATGGACAGATATGTATGGTTGA
TAGTATCGCAGTGGCTCTCAACGGTTAATACTCAATTATACAATAAAA
GAAAGAACATGTACAATGCTTAAATAATCAATCACAGCAATAGAAAAAA
TAATAGAACATATAATAGATATAGTGAAGAAGATAAAATGAATAT
TAACATTGATTAAATGATATAGATTAAACTTAATCAAAGTATAAATT
TAGCAATAAACATATAGATGATTATAAACCAATGTTCTATATCATAT
CTAATGAATAGAACATGATTCCATTAGCTGAAAAAGTTAAAGACTTTG
ATGATAATCTAACAGAGATTATTGGAGTATAGATAACAAATGAAC
ATATTACTTGATGAAGTAAATATTCTAAAGTAAATAGACAC
CTAAAAGACAGTATACCATTGATCTTCACTATATACCCtaa

B: BoNTG(H_n) encoded protein SEQ ID NO: 32

MAKNTGKSEQCIIVNNEDLFFIANKDSFSKDLAKAETIAYNTQNNTIENNFSI
DQLILDNDLSSGIDLPNENTEPFTNFDDIDIPVYIKQSALKKIFVDGDSLFEYL
HAQTFPSNIENLQLTNSLNDALRNNNKVYTFFSTNLVEKANTVVGASLFVN
WVKGVIDDFTSESTQKSTIDKVSDVSIIPYIGPALNVGNETAKENFKNAFEIG
GAAILMEFIPELIVPIVGFFTLESYVGNKGHIIMTISNALKKRDQKWTDMYGL
IVSQWLSTVNTQFYTIKERMYNALNNQSQAIEKIIEDQYNRYSEEDKMNINI
DFNDIDFKLNQSINLAINNDDFINQCSISYLMNRMPILAVKKLKDFDDNLKR
DLLEYIDTNELYLLDEVNILSKVNRHLKDSIPFDLSLYT*

FIGURE 18

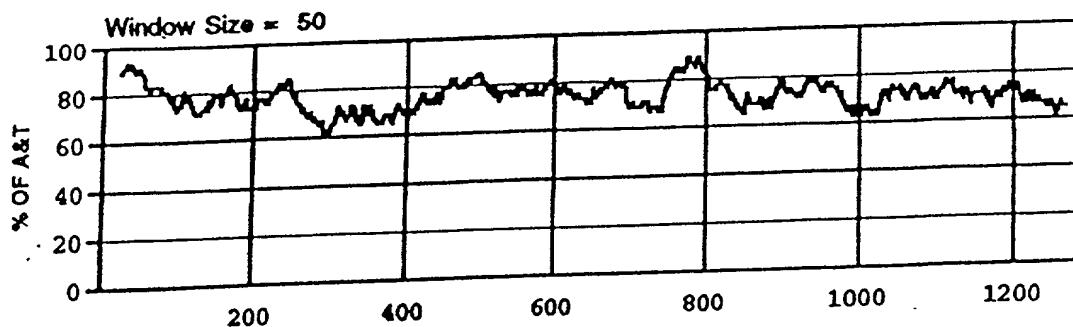
A: First BoNTF(Hc) gene: SEQ ID NO: 33

GAATTCACGatgTCTTACACTAACGACAAAATCCTGATCCTGTACTTCAAC
AAACTGTACAAAAAAATCAAAGACAACCTATCCTGGACATGCGTTACG
AAAACAACAAATTCATCGACATCTCTGGCTATGGTTCTAACATCTATC
AACGGTACGTCTACATCTACTCTACTAACCGCAACCAGTCGGTATCTA
CTCTCTAAACCGTCTGAAGTAAACATCGCTCAGAACAAACGACATCATCT
ACAACGGTCGTTACCAAGAACCTCTATCTCTTCTGGGTTCGTATCCCG
AAATACTTCAACAAAGTTAACCTGAACAACGAATAACACTATCATCGACT
GCATCCGTAACAACAACACTCTGGTGGAAAATCTCTGAACACTACAACAA
AATCATCTGGACTCTGCAGGACACTGCTGGTAACAACCCAGAAACTGGTT
TTCAACTACACTCAGATGATCTATCTCTGACTACATTAATAATGGAT
CTTCGTTACTATCACTAACAAACCGTCTGGGTAACACTCTCGTATCTACATCA
ACGGTAACCTGATCGATGAAAAATCTATCTCAACCTGGGTGACATCCA
CGTTCTGACAACATCCTGTTAAAATCGTTGGTCAACGACACCGGTT
ACGTTGGTATCCGTTACTTCAAAGTTTCGACACTGAACACTGGGTAAAAGT
GAAATCGAAACTCTGACTCTGACGAACCGGACCCGTCTATCCTGAAAG
ACTTCTGGGTAACTACCTGCTGTACAACAAACGTTACTACCTGCTGAAC
CTGCTCCGGACTGACAAATCTATCACTCAGAACTCTAACCTCCTGAACAT
CAACCAGCAGCGTGGTGTATCAGAAACCTAATATCTCTCTAACACTC
GTCTGTACACTGGTGTGAAGTTATCATCCGTTAAAACGGTTCTACTGAC
ATCTCTAACACTGACAACCTCGTACGTAAAACGACCTGGCTTACATCAA
CGTTGTTGACCGTGACGTTGAATACCGTCTGTACGCTGACATCTCTATCG
CTAAACCGGAAAAAAATCATCAAACGTTACTCTCTAACACTCTAACAA
CTCTCTGGGTCAGATCATCGTTATGGACTCGATCGGTAAACAACACTGCACTA
TGAACCTCCAGAACAAACAACCGTGGTACATCGGTCTGCTGGGTTCCA
CTCTAACAAACCTGGTTCTCTCATGGTACTACAACAAACATCCGTAAAAA
ACACTTCTTCTAACGGITGCTTCTGGCTTCTAAAGAACACCGGTT
GGCAGGAAAACtaaGAATT

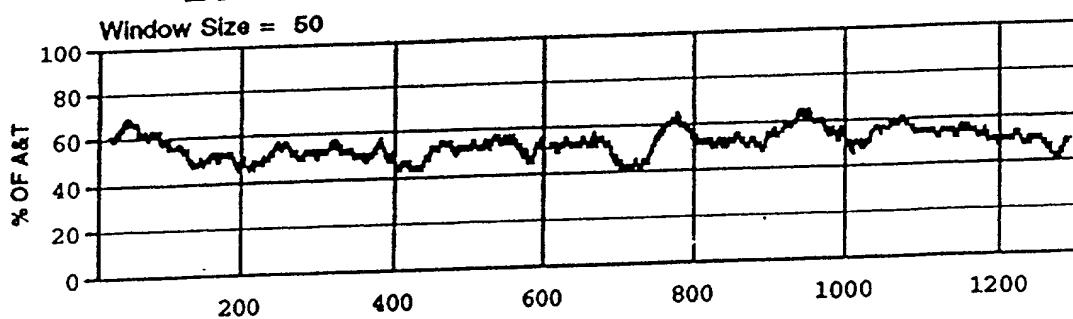
B: BoNTF(Hc) #1 encoded protein: SEQ ID NO: 34

MSYTNDKILILYFNKLYKKIKDNSILDMDRYENNKFIDISGYGSNISINGDVYIY
STNRNQFGIYSSKPSEVNIAQNDIYNGRYQNFSISFWVRIPKYFNKVNLNN
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNYTQMISISDYIN
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVDNIFKIVGCNDTRYV
GIRYFKVFDTELGTEIETLYSDEPDPSILKDFWGNYLLYNKRYYLLNLLRT
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIUKLIRTSNSNNSLGQIIVMDSI
GNNTMNFQNNNGGNIGLLGFHSNNLVASSWYNNIRKNTSSNGCFWSFIS
KEHGWQEN*

A: Natural BoNTF(Hc) Gene



B: First BoNTF(Hc) Synthetic Gene



C: Second BoNTF(Hc) Synthetic Gene

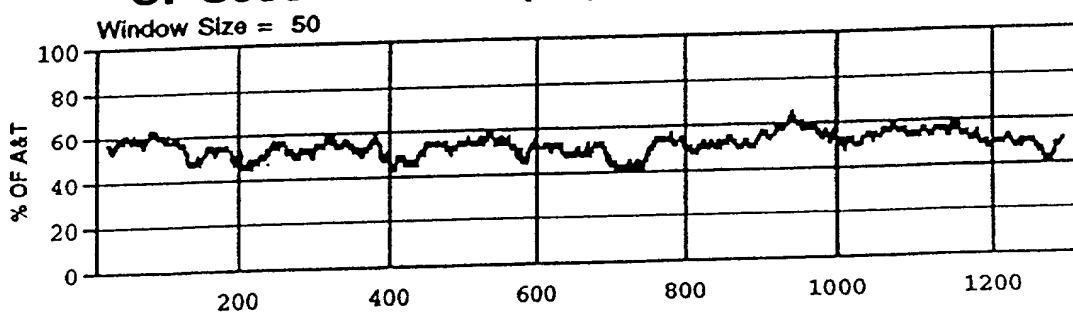


Fig 19

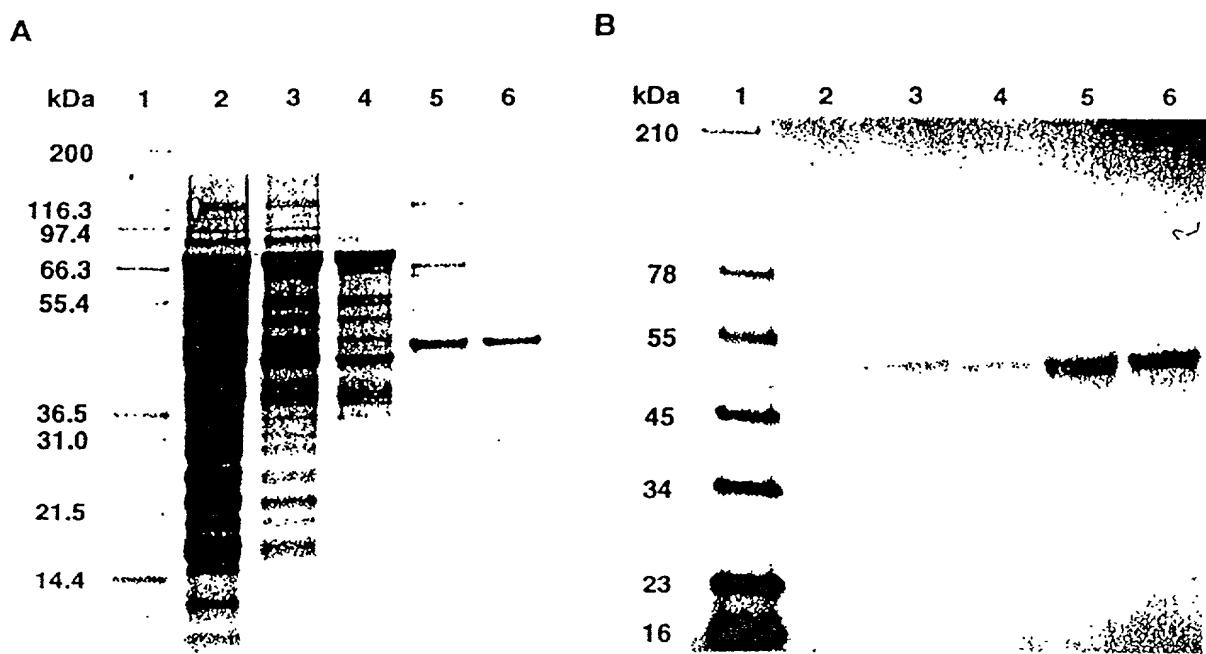


Fig 20

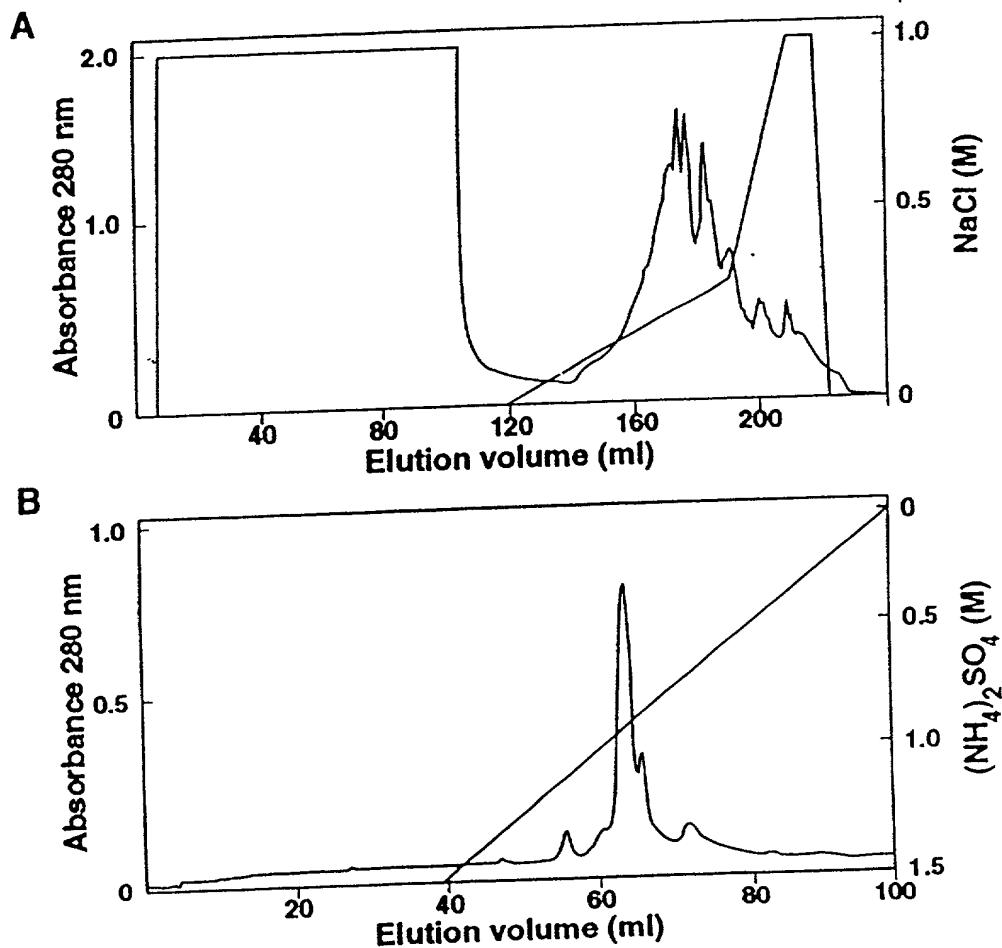


Fig 21

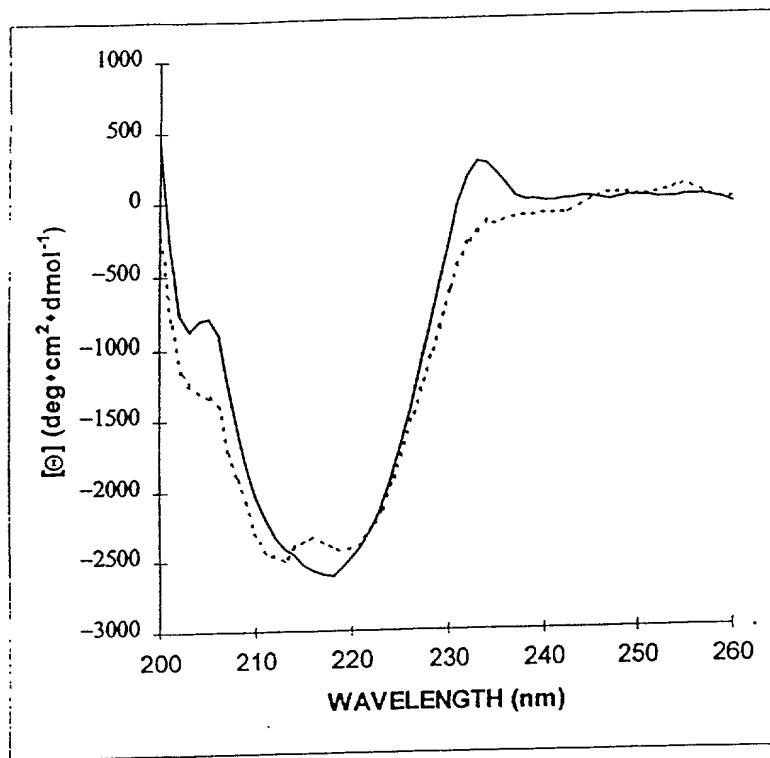


Fig 22